under (1) 35 USC §112, first paragraph, as nonenabled; and (2) 35 USC §112, second paragraph as indefinite (claims 24-33). These rejections are believed to be overcome in part by the above amendments and are otherwise traversed for reasons discussed below.

Applicants acknowledge the withdrawal of the objection regarding typographical errors as well as the withdrawal of the §112, first paragraph rejection of claim 4 set forth at pages 2-3 of the previous Office Action (Paper No. 8).

Overview of the Above Amendments:

Claims 24, 26 and 31 have been cancelled. Cancellation of these claims is without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more related applications toward the cancelled claims.

Claims 1, 9, 25, 27 and 29 have been amended. In particular, claims 1 and 9 now recite that the keratinocyte growth factor fragment "lacks the first 23 N-terminal amino acid residues of the mature, full-length keratinocyte growth factor but retains the remainder of the molecule." Claim 25 has been amended to incorporate language from now cancelled claim 26 and to recite the converse substitutions. New claim 34 corresponds to cancelled claim 24 and recites that the keratinocyte growth factor fragment has "the amino acid sequence depicted at amino acid residues 24 to 163, inclusive, of Figure 1." Finally, claims 25, 27 and 29 have all been amended to depend from new claim 34 instead of cancelled claim 24.

Support for the amendments and the new claim can be found in the claims as filed as well as throughout the specification at, *inter alia*, pages 6-7, bridging paragraph.

Thus, no new matter has been added to the application by way of the amendments. A copy of the currently pending claims, incorporating the amendments made herein, is appended for the Examiner's convenience.

Rejection Under 35 USC §112, Second Paragraph:

Claims 24-33 were rejected under 35 USC §112, second paragraph, as being indefinite. In particular, the Examiner notes that applicants refer to both Sequence Identification Number 1 and Figure 1 in claim 24 but that the two sequences use a different amino acid numbering system. The Action also objects to the use of the term "corresponding" in the claims. Applicants have cancelled claim 24 and submitted new claim 34 which refers only to Figure 1 and eliminates the term "corresponding." Hence, this basis for rejection is believed to be overcome.

Rejection under 35 USC §112, First Paragraph:

Claims 1-4, 9 and 24-33 were rejected under 35 USC §112, first paragraph. The Action alleges that "the disclosure is enabling only for claims limited to $KGF_{des1-23}$." Office Action, page 3, first full paragraph. The Action further asserts:

> [C]laim 1 encompasses numerous KGF fragments such as, for example, the single amino acid 24 of mature KGF, KGF fragments lacking both N-terminal and C-terminal amino acids, and KGF fragments lacking the first 23 amino acids and containing alterations in the remaining structure.

Office Action, page 4, first paragraph. However, applicants submit that the claims as amended recite an invention that is indeed enabled.

In particular, amended claims 1 and 9 now recite that the KGF fragment "lacks the first 23 N-terminal amino acid residues of the mature, full-length keratinocyte growth

factor but retains the remainder of the molecule." Hence, the Examiner's concerns stated above are believed to be obviated.

Additionally, the Action objected to the recitation of both Figure 1 and Sequence Identification Number 1 in the claims since the two sequences were numbered differently (see the §112, second paragraph rejection discussed above). However, as described above, claim 24 has now been substituted with claim 34 which refers only to Figure 1. Thus, this basis for rejection is believed to be overcome.

The Action also maintained that analogs, presumably as recited in claims 25-28, 30, 32 and 33, were not enabled. The Action states:

> Evidence can also be found in the art that conservative amino acid substitutions often result in loss of activity in a variety of proteins. Since the specification provides no guidance as to which amino acid residues of KGF can be substituted without affecting activity, claiming analogs of KGF is tantamount to an invitation to the skilled artisan to use the current invention ($KGF_{des1-23}$) as a starting point for further experimentation. Simply requiring in the claims and in the definitions provided by the specification that the resulting fragments and analogs of KGF must retain activity does not in itself provide guidance to the skilled artisan regarding which of the many KGF fragments and analogs could be constructed which would be expected to retain activity, without practicing undue experimentation.

Office Action, page 5. However, applicants believe that analogs of KGF, as claimed, are indeed enabled.

In this regard, claims 25, 27, 28, 30, 32 and 33 all specify the amino acids which may be substituted. Figure 1 of the application depicts a representative KGF amino acid sequence and shows the location of the recited amino acids. The specification provides assays for determining the ability of the KGF molecule to stimulate epithelial cell proliferation, a measure of KGF activity.

See, e.g., pages 10-11 and Example 5C (pages 38-39) of the application. Thus, one of skill in the art could readily make one or more of the specified substitutions, using routine methods known at the time of the invention, and test the analogs for KGF activity using the assays described in the specification. Contrary to the Examiner's assertions, applicants need not specify each and every analog of KGF that retains activity in order to enable the claims since to make particular analogs and to test for such activity would not constitute undue experimentation. The Examiner is reminded that enablement is not precluded even if some experimentation is necessary and that a patent need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986).

Indeed, as explained to the Examiner in the previous response, the Board of Patent Appeals and Interferences has addressed the issue of specified amino acid substitutions:

> "[t]he fact that a given protein may not be amenable for use in the present invention in that the cysteine residues are needed for the biological activity of the protein does not militate against a conclusion of enablement. One skilled in the art is clearly enabled to perform such work as needed to determine whether the cysteine residues of a given protein are needed for retention of biological activity."

In re Mark, 12 USPQ2d 1904, 1907 (BOPAI 1989). Thus, as in *Mark*, the specified substitutions could be readily made and the ensuing molecule for activity without undue experimentation. Nothing more is required by 35 USC §112, first paragraph regarding enablement.

Thus, applicants respectfully submit that they have met their duty and request the Examiner to reconsider and

withdraw the objection to the specification and the rejection of the claims under 35 USC §112, first paragraph.

Conclusion

Applicants respectfully submit that the claims comply with the requirements of 35 USC §112 and define an invention which is novel and nonobvious over the prior art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further communications in this application to the undersigned at:

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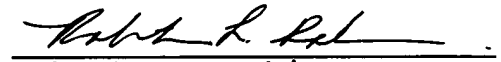
By: 
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